# 510(k) Summary
# diaDexus PLAC™ Test

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K050523

### *General Information*

| | |
|---|---|
| **Name and Address of Applicant:** | diaDexus, Inc.<br>343 Oyster Point Blvd.<br>South San Francisco, CA 94080 |
| **Device Trade Name:** | diaDexus PLAC™ test |
| **Generic Name:** | Enzyme Immunoassay for the Quantitative Determination of Lp-PLA2 (Lipoprotein-Associated Phospholipase A2) in Human Plasma |

### *Intended Use*

The diaDexus PLAC™ test is an enzyme immunoassay for the quantitative determination of Lp-PLA2 (lipoprotein-associated phospholipase A2) in human plasma, to be used in conjunction with clinical evaluation and patient risk assessment as an aid in predicting risk for coronary heart disease, and ischemic stroke associated with atherosclerosis.

### *Device Description*

The diaDexus PLAC™ test kit contains Lp-PLA2 calibrators, monoclonal anti-Lp-PLA2 (4B4) antibody conjugated to horseradish peroxidase, monoclonal anti-Lp-PLA2 (2C10) antibody-coated microwell strips with a stripwell frame, various buffers and related reagents, and a package insert. Each stripwell can be used for performing only one set of tests (i.e. single use). One plate may accommodate up to 40 clinical samples when assayed in duplicate. The kit expiration date and storage conditions are indicated on the package.

The diaDexus PLAC™ test is based on the standard principle of a sandwich enzyme immunoassay using two specific monoclonal antibodies. A set of Lp-PLA2 calibrators is used to plot a standard curve of absorbance (y-axis) versus Lp-PLA2 concentration in ng/mL (x-axis) from which the Lp-PLA2 concentration in the test sample can be determined. The concentration of Lp-PLA2 in each sample and control is then interpolated from the standard curve using a point-to-point curve fit with appropriate calibration curve fitting software.

***Characterization of Rare Reagents***

**Antigen**

The antigen used in the diaDexus enzyme immunoassay PLAC™ test is purified recombinant Lp-PLA2 (DDX-RA). Antigen preparations were characterized using SDS-polyacrylamide gels under reducing and non-reducing conditions and Western blot analysis using an anti-Lp-PLA2 antibody, to demonstrate consistency with the molecular weight of the antigen reported in the literature.

**Antibodies**

The monoclonal anti-Lp-PLA2 antibodies used in the preparation of the coated microwell strips (2C10) and conjugate (4B4) were characterized for purity and reactivity in a series of procedures including Paragon gel electrophoresis, SDS-PAGE, size exclusion chromatography, isotyping and enzyme immunoassay. These results demonstrated that the monoclonal antibodies bind to the Lp-PLA2 antigen quantitatively and specifically.

***Performance Characteristics – Analytical***

**Analytical Sensitivity (Detection Limit)**

The minimum detection limit, as calculated by interpolation of the mean plus two standard deviations of 24 replicates of the 0 ng/mL Lp-PLA2 calibrator, is 1.3 ng/mL.

**Linearity/Assay Range**

90 – 897 ng/mL

**Interfering Substances**

No appreciable interference from the addition of the following substances at the noted concentrations:

- Hemoglobin – 500 mg/dL
- Triglycerides – 3,000 mg/dL
- Cholesterol – 500 mg/dL
- Bilirubin – 20 mg/dL
- Albumin – 6.2 g/dL*
- Aspirin – 50 mg/dL
- Tylenol® – 20 mg/dL
- Vitamin C – 50 mg/dL
- Benadryl® – 50 mg/dL
- Orinase – 100 mg/dL
- Pravachol® – 446 µg/dL

* 2.3 g/dL albumin added to a plasma pool of presumptively 4 g/dL albumin

**Precision**

Intra-assay precision (n=80) ranged from 4.3 %CV to 5.8 %CV throughout assay range;

Inter-assay precision (n=20) ranged from 6.3 %CV to 8.7 %CV throughout assay range.

***Performance Characteristics – Clinical***

A clinical study was conducted to determine the efficacy of the diaDexus PLAC™ test as a predictor of risk for ischemic stroke associated with atherosclerosis. In this case-cohort study, Lp-PLA2 levels were evaluated in 956 banked EDTA-plasma samples from a large, multi-center, observational epidemiology study sponsored by the National Institutes of Health's National Heart, Lung, and Blood Institute, conducted in the United States (the ARIC study). Participants entered the study free of stroke and were followed for the development of stroke for up to nine years. Of the 956 participants selected for the Lp-PLA2 study, 194 subsequently suffered an ischemic stroke as defined by the ARIC investigators (cases) and 762 were stroke-free at the time of censor (controls). Cox regression models were used to evaluate the association of Lp-PLA2 and stroke in a univariate analysis (Model 1), a univariate analysis adjusted for demographics (Model 2), a multivariate analysis adjusted for demographics, diabetes, LDL, HDL, blood pressure, smoking status, body mass index (BMI), and CRP (Model 3), and all factors including CHD status (Model 4). Using tertile cutpoints of Lp-PLA2, the hazard ratios of the Cox regression analyses demonstrate that Lp-PLA2 is a significant predictor of time to stroke for the 3$^{rd}$ tertile (3T) when compared to the 1$^{st}$ tertile (1T) (Table 1). These data support the clinical utility of the diaDexus PLAC™ test to be used as a predictor of risk for ischemic stroke associated with atherosclerosis,

even after adjustment for traditional risk factors, other inflammatory biomarkers, and CHD status.

**Table 1**
**Results of the Cox Regression Analysis**

| Analysis | Risk Ratio 3T vs. 1T (p value) |
|---|---|
| Model 1 (univariate analysis) | 1.79 (p=0.0010) |
| Model 2 (adjusted for age, race and gender) | 2.09 (p=0.0001) |
| Model 3 (adjusted for age, race, gender, diabetes, LDL, HDL, blood pressure, smoking, BMI and CRP) | 1.81 (p=0.0034) |
| Model 4 (adjusted for age, race, gender, diabetes, LDL, HDL, blood pressure, smoking, BMI, CRP, and CHD status) | 1.75 (p=0057) |

***Conclusions***

1. Analytical: previous 510(k) clearances have demonstrated the acceptable analytical performance of the PLAC™ test.

2. Clinical: data were collected from a large, multi-center, observational epidemiology study sponsored by the National Institutes of Health, following a well-designed protocol conducted by qualified experts in a CLIA-certified laboratory. The results of this clinical study and performance testing demonstrate that the levels of Lp-PLA2 are associated with increased risk, and support the safety and effectiveness of the PLAC™ test for use as a predictor of risk for ischemic stroke associated with atherosclerosis.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 15 2005

Robert L. Wolfert, Ph.D.
Vice President of Diagnostics
diaDexus, Inc.
343 Oyster Point Blvd.
South San Francisco, CA 94080

Re: k050523
Trade/Device Name: diaDexus PLAC™ test
Regulation Number: 21 CFR 866.5600
Regulation Name: Low-density lipoprotein immunological test system
Regulatory Class: Class II
Product Code: NOE
Dated: April 28, 2005
Received: April 29, 2005

Dear Dr. Wolfert:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Carol C. Benson

Carol C. Benson, M.A.
Acting Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

# INDICATION FOR USE

**510(k) Number:** K050523

**Device Name:** diaDexus PLAC™ test

**Indications for Use:**

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Prescription Use __X__ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Carol C Benson
Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k) K050523